(*1*) For all tests except sterility: A minimum of 10 immediate containers.

(*2*) For sterility testing: 20 immediate containers, collected at regular intervals throughout each filling operation.

(b) *Tests and methods of assay.* Thaw the sample as directed in the labeling. he sample solution used for testing must be at room temperature.

(1) *Oxacillin content.* Proceed as directed in § 440.249a(b)(1), except use the thawed solution.

(2) *Sterility.* Proceed as directed in § 436.20 of this chapter, using the method described in paragraph (e)(1) of that section.

(3) *Pyrogens.* Proceed as directed in § 436.32(a) of this chapter, except inject a sufficient volume of the undiluted solution to deliver 20 milligrams of oxacillin per kilogram.

(4) *pH.* Proceed as directed in § 436.202 of this chapter, using the undiluted solution.

[55 FR 279, Jan. 4, 1990; 55 FR 2481, Jan. 24, 1990]

§ 440.255 Penicillin G benzathine injectable dosage forms.

§ 440.255b Sterile penicillin G benzathine suspension.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Sterile penicillin G benzathine suspension is an aqueous suspension of penicillin G benzathine and one or more suitable suspending or dispersing agents, buffer substances, and preservatives. Each container or each milliliter contains penicillin G benzathine equivalent to not less than 300,000 units of penicillin G. Its potency is satisfactory if it is not less than 90 percent and not more than 115 percent of the number of units of penicillin G that it is represented to contain. It is sterile. It is nonpyrogenic. Its pH is not less than 5.0 and not more than 7.5. The penicillin G benzathine used conforms to the standards prescribed by § 440.55a(a)(1).

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(*a*) The penicillin G benzathine used in making the batch for potency, moisture, pH, penicillin G content, and crystallinity.

(*b*) The batch for potency, sterility, pyrogens, and pH.

(ii) Samples required:

(*a*) The penicillin G benzathine used in making the batch: 10 packages, each containing approximately 300 milligrams.

(*b*) The batch:

(*1*) For all tests except sterility: A minimum of 10 immediate containers.

(*2*) For sterility testing: 20 immediate containers, collected at regular intervals throughout each filing operation.

(b) *Tests and methods of assay*—(1) *Potency.* Use either of the following methods; however, the results obtained from the iodometric assay shall be conclusive.

(i) *Microbiological agar diffusion assay.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Using a suitable hypodermic needle and syringe, remove all of the withdrawable contents if it is represented as a single-dose container; or, if the labeling specifies the amount of potency in a given volume, remove an accurately measured representative portion from each container. Dilute the portion thus obtained with sufficient absolute methyl alcohol to give a solution of convenient concentration. Immediately further dilute with 1 percent potassium phosphate buffer, pH 6.0 (solution 1), to the reference concentration of 1.0 unit of penicillin G per milliliter (estimated).

(ii) *Iodometric assay.* Using a suitable hypodermic needle and syringe, remove all of the withdrawable contents if it is represented as a single-dose container; or if the labeling specifies the amount of potency in a given volume, remove an accurately measured representative portion from each container. Using the sample thus obtained, proceed as directed in § 436.204(b)(2) of this chapter.

(2) *Sterility.* Proceed as directed in § 436.20 of this chapter, using the method described in paragraph (e)(2) of that section, except use medium C in lieu of medium A, and medium F in lieu of

medium E. During the period of incubation, shake the tubes at least once daily.

(3) *Pyrogens.* Proceed as directed in § 436.32(d) of this chapter, using a solution containing 4,000 units of penicillin G per milliliter.

(4) [Reserved]

(5) *pH.* Proceed as directed in § 436.202 of this chapter, using the undiluted sample.

[42 FR 59868, Nov. 22, 1977, as amended at 43 FR 9799, Mar. 10, 1978; 50 FR 19918, 19919, May 13, 1985]

§ 440.255c Sterile penicillin G benzathine-penicillin G procaine suspension.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Sterile penicillin G benzathine-penicillin G procaine suspension is an aqueous mixture of penicillin G benzathine and penicillin G procaine with or without suitable and harmless buffer substances, suspending agents, and preservatives. Each container or each milliliter contains penicillin G benzathine and penicillin G procaine each equivalent to not less than 150,000 units of penicillin G. Its penicillin G benzathine content is satisfactory if it is not less than 90 percent and not more than 115 percent of the number of units of penicillin G that it is represented to contain. Its penicillin G procaine content is satisfactory if it is not less than 90 percent and not more than 115 percent of the number of units of penicillin G that it is represented to contain. It is sterile. It is nonpyrogenic. Its pH is not less than 5.0 and not more than 7.5. The penicillin G benzathine used conforms to the standards prescribed by § 440.55a (a)(1). The penicillin G procaine used conforms to the standards prescribed by § 440.74a(a)(1).

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(*a*) The penicillin G benzathine used in making the batch for potency, moisture, pH, penicillin G content, and crystallinity.

(*b*) The penicillin G procaine used in making the batch for potency, moisture, pH, penicillin G content, and crystallinity.

(*c*) The batch for penicillin G benzathine content, penicillin G procaine content, sterility, pyrogens, and pH.

(ii) Samples required:

(*a*) The penicillin G benzathine used in making the batch: 10 packages, each containing approximately 500 milligrams.

(*b*) The penicillin G procaine used in making the batch: 10 packages, each containing approximately 500 milligrams.

(*c*) The batch:

(*1*) For all tests except sterility: A minimum of 10 immediate containers.

(*2*) For sterility testing: 20 immediate containers, collected at regualr intervals throughout each filling operation.

(b) *Tests and methods of assay*—(1) *Potency*—(i) *Total potency.* Assay for total potency by either of the following methods; however, the results obtained from the iodometric assay shall be conclusive.

(*a*) *Microbiological agar diffusion assay.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Using a suitable hypodermic needle and syringe, place one dose of the drug in a 100-milliliter volumetric flask and add sufficient methyl alcohol to dissolve the benzathine penicillin G. Dilute to volume with 1 percent potassium phosphate buffer, pH 6.0 (solution 1), and shake well. Immediately further dilute an aliquot with solution 1 to the reference concentration of 1.0 unit of penicillin G per milliliter (estimated).

(*b*) *Iodometric assay.* Proceed as directed in § 436.204 of this chapter, preparing the sample as follows: Using a suitable hypodermic needle and syringe, withdraw 2 one-dose portions of sample. Place one portion into an appropriate-sized volumetric flask and add 20 milliliters of 0.5*N* NaOH for each 300,000 units of benzathine penicillin G, mix well, being sure that all penicillin is in solution, and allow to stand for 15 minutes. Add 1 milliliter of 1.2*N* HCl for each 2 milliliters of 0.5*N* NaOH,